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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/965,807	10/01/2001	Reuben Matalon	SHUTT-1 C1	3645

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EXAMINER	
MAYER, SUZANNE MARIE	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/965,807	MATALON ET AL.	
	Examiner	Art Unit	
	Suzanne M. Mayer	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,22-24,66-75 and 80-82* is/are pending in the application.

4a) Of the above claim(s) *76-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,22-24,66-75 and 80-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 February 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on 19 April, 2004 is acknowledged. The traversal is on the ground that it would not be an undue search burden for the examiner to search Group II as well. This is not found persuasive because Group I and Group II are independent and patently distinct entities which would require separate and distinct searches. This would place an undue burden of search upon the examiner because antibodies are encoded by completely different DNA than an enzymes which increase the cost and time of examination.

The requirement is still deemed proper and is therefore made FINAL.

Drawings

2. The drawings, Figures 3 and 6, are objected to under 37 CFR 1.83(a) because they fail to show in clear and discernable fashion the gel pictures as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be

removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Information Disclosure Statement

3. The information disclosure statement filed 12/18/2001 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

4. Claims 70-72 and 75 are objected to because of the following informalities: the claims are substantial duplicates of one another. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 20, 22, 67-75 and 81-82 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20, 22, 67-75 and 81-82 are rejected as being indefinite in the use of the phrase 'normal human aspartoacylase' or 'normal aspartoacylase'. What constitutes 'normal' is indefinite. The use of the phrase 'wild-type', which is common in the art when referring to non-altered polypeptides expressed either naturally or recombinantly, would clarify this ambiguity.

Claim 22 is further rejected for several reasons: i) the word 'having' in the first line is misspelled, ii) it recites the limitation "said mutation" in the fourth line. There is insufficient antecedent basis for this limitation in the claim since the definition of the mutation follows the use of the phrase 'said mutation', iii) the phrase 'allelic variant' is an indefinite term because there are no criteria for establishing whether an allelic variant even exists. An allele is the same gene on the other copy of the chromosome but assuming it did exist may not manifest its characteristics in an identifiable phenotype if it the characteristic of that gene being examined is not a dominant characteristic. Therefore, the establishment of what constitutes an allelic variant is indefinite.

Claims 24, 66 and 82 are included in this rejection as these claims depend from the rejected claims above and do not further the ambiguity.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 22, 66, 68-75 and 80 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claim 22 reads on an isolated human aspartoacylase according to SEQ ID NO:2 except with mutations at E285A, Y231X and/or A305E, or an allelic variant of said mutant aspartoacylase. The claim is rejected because exactly what constitutes an allelic variant of said mutant aspartoacylase is very broad and unspecific. Because an allelic variant is an alteration in the normal sequence of a gene, the significance of which is often unclear until further study of the genotype and corresponding phenotype occurs in a sufficiently large population, it is clear from the specification that Applicant did not have possession of all possible allelic variants of the mutant aspartoacylase at the time the application was filed.

Claims 66, 68-75 and 80 are drawn to fragments or polymorphic forms of human aspartolacylase pertaining to claims 66, 68-75 and 80. The claims do not require that

the fragments or polymorphic forms of the polypeptide possess any particular biological activity or other disclosed distinguishing feature. Thus, the claims are drawn to an undefined genus of fragments of amino acids with the only potential to recognize them being by sequence identity or hybridization ability or generation of antibodies.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factors present in claims 66, 68-75 and 80 is the partial structure or variants thereof. There is not even identification of any particular portion of the structure which might be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description.

Vas-Cath Inc. V. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." As discussed above, the skilled artisan cannot envision the detailed structures of fragments or variants thereof pertaining to the polypeptide of Seq ID No. 2 or human aspartoacylase, and therefor conception is not achieved until reduction to

practice has occurred, regardless of the complexity or simplicity of the methods of making the claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating or making it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

7. Claims 66, 68-75 and 80 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 66, 68-75 and 80 read on fragments or polymorphic forms of human aspartoacylase according to SEQ ID No:2. Thus, the claims read on any portion of this protein's sequence in reference to fragments, and any sort of substitution, deletion or insertion which does not alter the function of the protein in regards to polymorphic forms. The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not enabling for claims drawn to fragments and polymorphic forms for SEQ ID No:2.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case: 1) the quantity of experimentation required to determine which fragments or polymorphic forms of SEQ ID No:2 has the claimed function is large due to the large number of possible fragments, 2) the amount of guidance given in the specification in order to make or use the claimed invention is applicable only to SEQ ID No:2 and not necessarily to the fragments and polymorphic forms of thereof, 3) the working examples are just a fraction of what might encompass fragments or polymorphic forms of SEQ ID No:2 because how fragments of SEQ ID No:2 perform in the given protocol is unclear, 4) the nature of the invention is such that it is non-trivial and requires considerable experimentation and time to produce possible fragments or

polymorphic forms of SEQ ID No:2 because of the vast combinations of possible fragments obtainable from SEQ ID No:2, 5) the state of the prior art does not aid one of ordinary skill in the art exactly what which fragments of polymorphic forms of SEQ ID No:2 will function the same as SEQ ID No:2, 6) the relative skill of those in the art is very high and 7) the predictability of which fragment will be an epitope is very small and 8) the breadth of the claims is considerably broad because the large variety of fragments of different sizes. Therefore, the claims as written would not allow one of ordinary skill in the art to reproduce, make and/or use the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Kaul et al.

Kaul et al. teach the isolation and purification of aspartoacylase from human and bovine brain using conventional column chromatography techniques. Since this aspartoacylase is capable of hydrolyzing N-acetyl-aspartic acid to aspartate and acetate, this meets the limitations of the claim.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suzanne M. Mayer, Ph.D whose telephone number is 571-272-2924. The examiner can normally be reached Monday-Friday 8.30am-5.00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Westbrook can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SMM
15 June, 2004

ROBERT A. WAX
PRIMARY EXAMINER